REMARKS

Claim 67 was amended to overcome the rejection under §112, second paragraph rejection, and as there are no remaining rejections of it, this claim appears to be in condition for allowance.

Drawings

Corrected drawings are attached.

Information Disclosure Statement

The references missing from the Information Disclosure Statement will be provided to the examiner in a separate enclosure.

Claim Objections

An Applicant has the right to restate the claimed invention in a reasonable number of ways. See, e.g., M.P.E.P. §706.03(K).

Rejections under §112, second paragraph

Claims 20, 22, 67-75, and 81-82 have been amended by replacing the term "normal" with the "wild-type." This amendment does not change the scope of the claims since the skilled worker would have understood these terms to have the same meaning. Support for the amendment can be found in the specification, e.g., Page 9, line 10; Figs. 5A and 6A (where "WT" is used as an abbreviation for wild-type).

Rejections under §112, first paragraph

Claim 22 has been amended to clarify that the claimed polypeptide includes a "naturally-occurring mutant allele of said wild-type human aspartoacylase" comprising the amino acid sequence SEQ ID NO:2. The phrase "naturally-occurring mutant allele" has its conventional meaning, e.g., to

indicate that it is a mutation associated with Canavan disease. See, e.g., Specification, Page 3, lines 24-28 and Page 11, lines 5-27. This amendment does not change the claim scope.

The specification provides at least three different examples of naturally-occurring mutant alleles, including mutations at amino acid positions 285, 231, and 305 of the wild-type aspartoacylase polypeptide. Additional mutations can be isolated without undue experimentation. For instance, at least seven different methods are disclosed in the specification for identifying mutations in patient samples, including direct sequencing, heteroduplex analysis, restriction digestion analysis, single strand conformation polymorphism (SSCP), enzymatic activity, and immunoassay. See, e.g., Specification, Page 22, line 21-Page 24, line 9. Examples 7, 11, and 12 describe the isolation of three different mutant alleles using a combination of PCR, direct sequencing, SSCP, and restriction digestion analysis. This information, coupled with the skilled worker's knowledge is adequate to satisfy the statutory requirements of §112, first paragraph.

The claims have also been amended to recite "a naturally-occurring polymorphic form" to clarify that the polymorphic form can be identified from a human patient sample. Contrary to the statements in the Office action, applicants clearly have possession of the claimed genus of polypeptides. The specification provides at least three examples of polypeptides that fall within it, and identify several conserved regions that reveal the "common attributes or features of the elements possessed by members of the genus." The latter was described in *University of California v. Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406, to be sufficient show possession of a genus, as well as by the PTO in its *Written Description Guidelines* to be the appropriate examination standard. *Synopsis of Application of Written Description Guidelines*, Page 39, last sentence; Example 13, Page 51. For example, conserved motifs that relate to enzyme activity are found at amino acid positions 18-24, 275-278, and 293-289. See, e.g., Fig. 2; Specification, Page 8, line 33-Page 9, line 4; Sequence Disclosure Statement. Consistently, the mutation at position 285 is associated with a loss of enzyme activity. Additionally, the nonsense mutation at position 231 codes for a truncated form of the enzyme that lacks two of the three functional regions, and predictably, has no aspartoacylase activity.

Furthermore, claims have been added to indicate that the claimed polypeptides are encoded by a nucleic acid which specifically hybridizes under stringent conditions to a nucleotide sequence of SEQ ID NO:1. Support for this amendment can be found, e.g., at Page 1, lines 28-Page 12, line 3; Page 14, lines 1-9. The PTO in its *Written Description Guidelines* has acknowledged that hybridization claims conform to the requirements of §112, first paragraph, and this position has been adopted in *Enzo v. Gen-Probe*, 296 F.3d 1316; 63 U.S.P.Q.2D 1609 (Fed. Cir. 2002). See, *Written Description Guidelines*, Example 6. Moreover, these *Guidelines* recognize the conventionality of hybridization conditions. ("The art indicates that hybridization techniques using a known DNA as a probe under highly stringent conditions were conventional in the art at the time of filing.")

Claims have also been amended to indicate that the fragments are "immunologically-effective to elicit antibodies that selectively bind to said human aspartoacylase." Support for this amendment can be found throughout the specification, e.g., on Page 17, lines 1-23. While this is not an acquiescence to the grounds of the rejection, it clearly provides "a biological activity or other disclosed distinguishing feature" that is described in the Office action as a basis for the rejection. See, Office action, line spanning Pages 5-6. The specification provides a number of examples of polypeptide fragments, including, e.g., SEQ ID NOS: 10-16, and 24-27. Methods for determining whether a fragment possesses the recited activity are conventional, as well as being described in the specification. See, e.g., Page 17, lines 1-23; Page 23, line 29-Page 24, line 9. Thus, the claims are fully described and enabled.

Rejection under §102

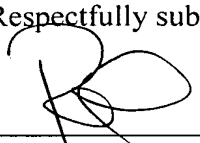
Kaul et al. do not describe a recombinant aspartoacylase. Nonetheless, claim 20 has been canceled without prejudice or disclaimer as being duplicative of other pending claims.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is

courteously invited to telephone counsel at the number indicated below.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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